People at ultra high risk for psychosis

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Chapter 4

The prevalence and structure of self-reported psychotic-like experiences in help-seeking mental health patients in the general population; a latent-class analysis

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Abstract

Latent class analyses in the general population have found that the psychosis phenotype has four classes. Could this be replicated in a sample of help-seeking people accessing mental health services for symptoms of non-psychotic mental disorders?

All patients (18-35 yrs old) referred for non-psychotic mental health problems to the secondary mental healthcare service in The Hague between February 2008 to February 2010 (N=3694), were included. Patients completed the Prodromal Questionnaire (PQ) and latent class analysis was applied to explore the number, size and symptom-profiles of the different classes.

The latent class analysis resulted in four classes. Subjects placed in Class 1 (N=448, 12.2%) endorsed almost all PQ-items, were more often diagnosed as psychotic or at high risk of developing psychosis, and were referred for treatment for posttraumatic stress and mood disorders. In Class 2 (N=1125, 30.3%) paranoia and mood symptoms were more prevalent. Subjects often meet criteria for the high risk group and were often diagnosed with mood disorders or personality disorders. Class 3 (N=1329, 36.2%) scored high on disturbed mood and anxiety and were treated for these symptoms. Class 4 (N= 792, 21.3%) represents the 'normative' group with low probabilities for all items. Subjects were more likely to be male and diagnosed with anxiety disorders, eating disorders and relationship problems. The results support the hypothesis that a representation in four classes of psychotic-like experiences can also be applied in a help-seeking population.

Keywords: psychosis continuum, prodromal symptoms.

Introduction

In recent studies, psychosis has been examined from a dimensional perspective, i.e. with psychotic symptoms on a continuum of severity, in contrast to the previous categorical or dichotomous perspective (Stip & Letourneau, 2009; Van Os, Hanssen, Bijl & Ravelli, 2000; Van Os, Linscott, Myin-Germeys, Delespaul & Krabbendam, 2009). The concept of a continuum is based on the observation that psychotic features are present in both healthy and psychiatric subjects and that psychotic disorder represents the extreme end of the continuum. The continuum hypothesis of psychosis is supported by the finding that the prevalence of psychotic experiences is 17.5 percent in the Dutch general population (Spauwen, Krabbendam, Lieb, Wittchen & Van Os, 2003; Van Os et al., 2000). The idea of a continuum is not supported by the lack of valid nosological diagnoses, because the continuum concept presupposes a single disease entity. For this reason it has been suggested to use the more 'agnostic construct' of extended phenotype, where psychotic-like experiences (PLEs) in the general population, if combined with suffering and reduced functioning, gradually blend into clinical disorders (Howes & Kapur, 2009; Kaymaz & Van Os, 2010).

Although a high number of PLEs is associated with help-seeking behavior and with a greater risk of developing psychosis (Yung et al., 2008), the number of subclinical psychotic experiences only partially explains the transition to full psychotic disorder. There are also differences in need for care, the quality of the symptoms and the associated distress (Yung et al., 2006). In 84% of a general population sample, PLEs disappeared over a two-year period and only eight percent had persistent PLEs; another eight percent developed full psychosis (Hanssen, Bak, Bijl, Vollenberg & Van Os, 2005). In a general adolescent sample followed for eight years, persistent PLEs were associated with a transition to psychotic disorder (Dominguez, Wichers, Lieb, Wittchen & Van Os, 2011). Therefore, PLEs are considered to be a behavioral expression of a (transient) risk factor for developing psychosis. Risk also increases with cannabis use, traumatic experiences and urbanicity (Cougnard et al., 2007).

The transient nature of PLEs might suggest that some PLEs are innocent phenomena not associated with psychosis, while others might be associated with ultra high risk for developing psychosis. This difference in outcome calls for a subdivision of PLEs, where some are more related to psychotic disorder than others. Several categories of PLEs might exist and this could be examined by latent class analysis (LCA). LCA is a statistical method to reduce heterogeneous groups in unmeasured, relative homogenous groups of patients using categorical observed

variables. LCA analyses empirically test for the existence of discrete groups with a similar item endorsement profile (Lazarsfeld & Henry, 1968; McCutcheon, 1987).
LCA of psychotic-like features in the general population and a high-risk population has shown repeatedly that four classes (in which the subjects in the different classes gradually endorsed PLEs) best fit the data and that the class endorsing the most psychotic items was the most associated with known risk factors and to psychopathology in general, while a normative class endorsed almost no items (Cella, Sisti, Rocchi & Preti, 2010; Murphy, Shevlin & Adamson, 2007; Shevlin, Murphy, Dorahy & Adamson, 2007; Valmaggia et al., 2011). Shevlin et al.(2007) named the classes: 'Psychosis' (N=105, 1.8%), 'Hallucinatory' (N=349, 6.0%), 'Intermediate' (N=343, 5.9%) and 'Normative' (N=5,057, 86.4%). So far, no research has been performed on the distribution of PLEs in a help-seeking population presenting to general secondary mental health services for non-psychotic disorders.
The current study explores the prevalence and the underlying latent structure of PLEs and other putative prodromal symptoms. The subjects are a consecutive sample of patients not considered to be psychotic, ages 18 to 35 years who sought help at secondary mental health care services in The Hague between February 2008 and February 2010. LCA was used to group subjects of the study population into homogeneous classes, to assess the validity of the clustering results, to interpret the classes found and to validate these against the risk of developing psychosis, the risk of psychosis, and the type of treatment that was indicated for their primary disorder. The results might contribute to an understanding of the etiology of psychosis - why some PLEs precede psychosis, whereas others do not – and may allow for prediction of groups that require different treatments.

Methods

This paper analyzes baseline data from the Dutch EDIE-trial, registered at Current Controlled Trials: number ISRCTN21353122. A comprehensive description of the study, aims, sample procedure, diagnostic instruments, randomization protocol, informed consent, quality control procedures and analysis has been described in a previous publication (Rietdijk et al., 2010). The design of this study has been approved by the Dutch Union of Medical-Ethics Trial Committees for mental health organizations. The trial was conducted in compliance with the 'Declaration of Helsinki' (amendment of Edinburgh, 2000).

Setting

The screening procedure was implemented in the secondary mental healthcare institution PsyQ Haaglanden, which is the main provider of the general adult mental healthcare for The Hague area. The Hague is a city in the Netherlands, with a catchment area that covers approximately 600,000 inhabitants. Yearly, approximately 5,000 (0.8%) inhabitants seek help for non-psychotic disorders in PsyQ; 44% (N=2,200) are between 18 and 35 years old and of these patients, almost 70% actually attend the intake procedure. Help-seeking individuals, who are referred by their GP's, are first screened by a telephone interview. Following this initial screening, patients are referred to one of the care programs for further assessment and diagnosis. Patients with a primary florid psychosis are referred to Parnassia Psychiatric Institute and were not included in the current study.

Sample

Between February 2008 and February 2010 all consecutive referrals (N=3,694) aged 18 to 35 to PsyQ Haaglanden, were screened with the Prodromal Questionnaire (PQ; Loewy, Bearden, Johnson, Raine & Cannon, 2005). The age group 14-35 years is considered to be the age with the highest risk of developing psychosis (DeLisi, 1992). However, PsyQ Haaglanden only provide adult care (18 years and above) and therefore we used the age criteria of 18-35 years.

Measures

The Prodromal Questionnaire (PQ) (Loewy et al., 2005) is a self-report questionnaire with 92 'true/false'-items on prodromal psychosis symptoms. Most items are modified from the Structured Interview for Prodromal Syndromes (SIPS; Miller et al., 2003) and the Schizotypal Personality Questionnaire (Raine & Benishay, 1991). Items are divided into four distinct groups: positive symptoms (N=45), negative symptoms (N=19), disorganized symptoms (N=13) and general symptoms (N=15). Positive symptoms are grouped in three sub-scales: 1) Unusual thought content, delusional ideas, and paranoia; 2) Perceptual abnormalities and hallucinations; and 3) Conceptual disorganization. Loewy et al. (2005) found good preliminary validity in detecting people with prodromal or psychotic status. The instrument was less sensitive to discriminating prodromal status from full-blown psychosis.

We used external criterion analysis to validate the resulting classes by comparing them to variables which were not used for the classification procedure, but were available for the subjects. We used type of care program to which the patient was assigned and the results of the assessment with the Comprehensive Assessment

of At Risk Mental States (CAARMS;Yung et al., 2005), which was conducted when a patient scored above the cut-off score of 18 on the positive symptom scale of the PQ (this cut-off score was an inclusion criterion for the EDIE.NL study; see for details, Rietdijk et al., 2010). The CAARMS is a semi-structured interview that assesses psychotic-spectrum symptoms that occurred during the last year before assessment. The frequency and intensity of the symptoms are assessed separately, which makes it possible to distinguish between at-risk mental states (ARMS), full psychosis and neither with a high sensitivity (86%), specificity (91%), positive predictive value (80%) and negative predictive value (94%). ARMS-scores on the CAARMS are predictive for the development of psychosis within one year with a relative risk of 12.44 (95% CI= 1.5 – 103.41, p= 0.0025) (Yung et al., 2005).
Social functioning of the subjects was drawn from the patient register which contains all patient information, including diagnosis and Global Assessment of Functioning (GAF; American Psychiatric Association, 1994)-scores determined by clinicians. The GAF rating has scores from 0 to 100. A score of 50 or below indicates serious problems with social functioning.

Analysis method
LCA was performed using Mplus version 6 (Muthén & Muthén, 2010). Demographics and distribution of PLEs on the PQ were explored using the Statistical Package for Social Science (SPSS), Version 18.
LCA was used to assess potential population heterogeneity (distinct groups of subjects) based on the presence or absence of symptoms in a population. LCA is a model-based cluster analysis based on Maximum Likelihood estimation methods which allows identification of homogeneous groups (latent classes) from categorical multivariate data (Everitt, Landua, Leese & Stahl, 2011; Lazarsfeld & Henry, 1968). This method assumes: 1) k latent classes underlying the dataset and 2) that each case belongs to only one class. Specifically, LCA assumes that the distribution of cases is generated by a mixture of probability distributions in the population from which the cases are drawn. The number of classes and their sizes are not known a priori. LCA is based on a statistical model and therefore objective model selection procedures for determining and testing the number of classes and its sizes exist (Everitt et al., 2011). If a model is selected in LCA, a case is assigned to the class with the highest posterior probability.
The best model is selected using several fit indices: likelihood ratio chi-square (LRc^2), Akaike information criterion (AIC), Bayesian information criterion (BIC), sample size adjusted BIC (SSABIC), Lo-Mendell Rubin's adjusted likelihood ratio

test (LRT) and entropy measures. Lower values of LRc^2, AIC, BIC and SSABIC suggest a better-fitting model. The Lo-Mendell-Rubin Likelihood ratio test compares a model with k against a model with k-1 clusters (Lo, Mendell & Rubin, 2001). A significant result suggests that the k+1 cluster solution is preferable. Entropy is an overall measure of how well a model predicts class membership, which ranges from 0 (no predictive power) to 1 (perfect prediction). Research on model selection criteria has not yet provided an unequivocal answer to the basic question of how to select the right number of components. Several authors therefore recommend the use of multiple statistics along with theoretical and practical considerations (Bauer & Curran, 2011; Nagin, 2005). An essential assumption of LCA is that of conditional independence, which requires that observed variables are statistically independent (uncorrelated) within each latent class. Violations can lead to models with additional spurious classes. The majority of bivariate associations (contingency coefficient) in this study between the binary variables were smaller than 0.3 (92.3%) and only 1.1% were larger 0.4% (max: 0.55), suggesting only minor problems with the assumptions of local independence.

The number of positive PLEs (the positive item scale of the PQ only) was explored using SPSS version 18. ANCOVA's were performed to measure whether sex, age and type of care program influenced the number of positive PLEs only. The number of positive items was tested as a predictor for at risk mental state on the CAARMS.

Chi-square tests and multinomial regression were performed to characterize the latent classes and to identify the clinical variables that best described class membership (Nagin, 2005; Tabachnick & Fidell, 2000).

Multinomial logistic regression was performed to validate the latent class solution derived against external variables, which were not used for the LCA. Multinomial logistic regression and chi-square analyses were used to assess associations between class membership and items, demographics and diagnosis.

Results

Demographic characteristics

The demographic characteristics of the sample are listed in Table 4.1. The respondents were predominantly female. Mean age was 26.42 (sd=5) years. Most of the patients received treatment at the anxiety and mood disorder departments. According to the case register of PsyQ, almost half of the patients (46.3%) had sought help previously and were diagnosed within PsyQ prior to the current event.

Distribution of Psychotic-like experiences

Almost all patients (N= 3,581; 96.9%) reported at least one item on the positive symptom scale of the PQ. The mean number of PLEs was 10.87 (se=.49) (see table 1). Analysis of variances (Anova's) were conducted to asses sex, age and care program on the number of PLEs and showed a significant main effect for sex (F (2, 3693) =5.95, p=.003) and care program (F (9, 3482) = 25.0, p<.0005). Women (M= 11.82, se=.16) reported more PLE's than men (M= 10.84, se=.24). Posthoc-test found that people with ADHD, mood disorders, personality disorders and PTSD, reported more PLEs than the subjects in the other care departments. No significant effect was found for age (F (21, 3693) = 1.45, p= .08).

Table 4.1: Demographic characteristics of the patient population

Care program	N	M (%)/F	Age Mean (SD)	Mean number of care events	PQ Positive symptoms Mean (SE)
Attention Deficit Hyperactive Disorder	463	240 (52%)/223	25.5(5.2)	1.9	12.37 (.40)
Anxiety disorders	923	324 (35%)/599	26.3 (4.8)	2.1	10.25 (.31)
Mood disorders	713	199 (28%)/514	27.3 (4.8)	2.4	12.83 (.43)
Eating disorders	177	11 (6%)/166	24.1 (5)	1.8	8.57 (.91)
Personality disorder	363	89 (24%)/274	25.9 (4.9)	2.8	13.66 (.55)
Relationship problems	418	119 (28%)/299	26.9 (5.2)	1.9	8.56 (.48)
Psychosomatic disorders	99	33 (33%)/66	28 (5.3)	2.3	10.91 (.96)
Sexual disorders	92	49 (53%)/43	28.5 (4.5)	2.7	6.56 (.96)
Posttraumatic Stress Disorder	235	39 (17%)/196	25.7 (4.9)	2.1	14.66 (.97)
Other disorders	209	75 (36%)/134	-	-	-
Missing cases	2				
Total	3694	1178 (32%)/2514	26.4 (5)	2.2	10.87 (.49)

Results of Latent Class Analysis

LCA models containing one to six classes were fitted to the data of all prodromal items. Table 4.2 displays the fit indices for each model. The three information criteria decrease with increasing number of clusters while the Lo-Mendell Rubin Test suggests a 3-class solution. The entropy was very high for all clusters. We therefore considered both 3 and 4 classes as best fitting solutions. However, further analyses showed that the 4 classes gave more clinically relevant information, as this solution was able to form a class with the persons that had the highest probabilities on all the PQ items. The posterior probabilities of the final class membership were all very high (0.962-1) meaning that there was little uncertainty in assigning a case to a class.

Table 4.2: Fit indices for the latent class analysis of psychotic-like experiences

	Number of classes					
	1	2	3	4	5	6
LL		-180403	-159951	-154311	-152498	-150811	-149753
Parameter		96	193	290	387	484	581
AIC		360998	320287	309203	305770	302590	300669
BIC		361595	321486	311005	308175	305598	304279
SSABIC		361290	320873	310083	306945	304060	302433
Entropy		N.A.	0.939	0.934	0.909	0.905	0.903
p		<0.0001	<0.0001	<0.0001	0.4149	0.042	0.1832
Class sizes							
1 class		3694	1771	1150	448	769	709
2 classes			1923	1677	1125	1006	439
3 classes				867	1329	638	791
4 classes					792	507	473
5 classes						774	760
6 classes							522

LL = Lo-Mendell Rubin likely-hood test; AIC = Akaike information criterion; BIC = Bayesian information criterion; SSABIC = sample size adjusted BIC.

Characterization of classes

Figure 4.1 displays the class-patterns. Class 1 was the smallest class (N=448, 12.2%) and was characterized by the highest probability of endorsing all symptoms (>.75). Compared to class 2, 3 and 4, patients in this class were more likely to endorse items of perplexity, paranoia, conceptual disorganization, withdrawal, avoliton, social anxiety, decreased expressed emotion, anxiety, mood problems and problems with stress regulation. With regard to PQ scores, this group was considered to be the group with the most severe symptoms and therefore was labeled 'severe'.

The pattern of class 2 (N=1125, 30.3%) showed lower probabilities of endorsing all the items compared to class 1. This pattern takes an intermediate place between class 1 and class 3. Subjects in class 2 had high endorsing rates (probability>.50) on paranoia, conceptual disorganization, perceptual abnormalities, avolition, reduced experience of emotion, disturbed sleep and problems with stress regulation. Due to these scores, the group was labeled as 'moderate'.

Class 3 was the largest group (N= 1329, 36.2%) and was labeled as 'mild'. Subjects in this class had a low probability of scoring on positive items of the PQ (probability >.25). However, the probabilities for endorsing negative symptoms, experienced emotion, disturbed mood and problems with stress regulation were elevated.

Class 4 (N=792, 21.3%) was characterized by almost zero probabilities of endorsing

the items and is referred as the 'normative' class. Patients in this class showed higher probabilities on depression and problems with stress regulation. There were no significant differences in age between the four classes F (3, 3650) = 0.63, p=.60.

Chi-square analyses on the items showed that all items significantly contributed to the distinction between the four classes. This is an indicator that the LCA is performed correctly; since all the items contributed to the defining of the classes and that the distinction between classes was not the result of the presence or absence of a small number of highly correlated symptoms. Analyses with total scores did not result in converging models with more than three classes and lower class solutions were only separated by one variable.

Validation of latent classes

Chi-square analyses and multinomial regression analyses were performed per class to compare the proportion of treatment program types and CAARMS diagnoses in each class to validate the results of the LCA. Table 4.3 shows the prevalence of treatment program types in the four classes and the odds ratios (OR), comparing the first three classes with the normative class (class 4).

If we look closer into the different diagnoses at initiation, the analyses show associations between treatment program types and classes. In class 1 the proportion of mood disorders, posttraumatic stress disorder and personality disorder is higher than in class 4. This overrepresentation remains after adjusting for sex in a multinomial regression with sex and care program type as independent and class membership as dependent variable. Class 2 is also characterized by a higher prevalence of mood disorder, PTSD and personality disorder. Subjects in class 3 and class 4 were more often help-seeking for relationship problems and less often treated for mood problems. Members of class 4 were more likely to have sexual problems than members of the other three classes.

Chi-square analyses were performed for class and differences in sex, outcome of the screening (meeting criteria for CAARMS-interview), the outcome of the CAARMS-interview (ARMS, psychotic and neither) and the GAF score (see table 4.4). More women than men did seek help for different disorders. There were significant differences between the four classes with males more likely to be in class 4.

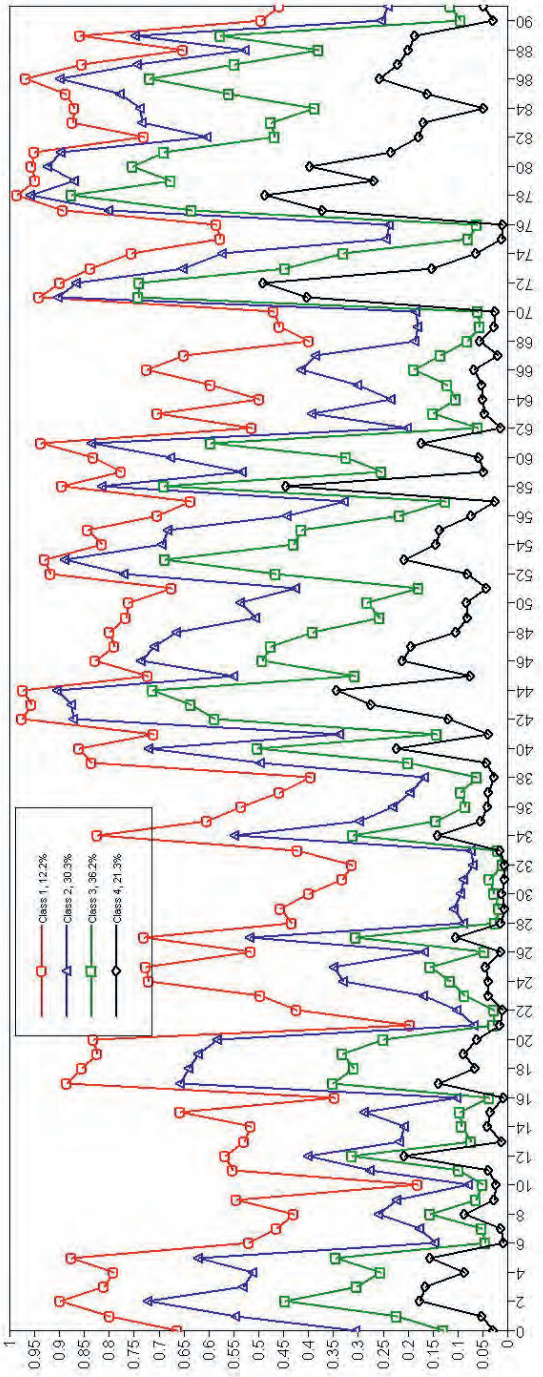
Table 4.3: Prevalences and odds ratios of care programs across the classes . Presented odds ratios are the odds of being in class 1 to 3 relative to the odds of class 4 (baseline).

Care program	Class 1: Severe N (percent) OR (95% CI)	Class 2: Moderate N (percent) OR (95% CI)	Class 3: Mild N (percent) OR (95% CI)	Class 4: Normative N (percent) OR (95% CI)	Chi-square (df=3)	P-value
ADHD OR	49 (10.9%) 0.82 (0.57-1.18)	130 (11.5%) 0.87 (0.66–1.15)	181 (13.6%) 1.05 (0.81-1.36)	103 (13%) 1.00	3.640	.303
Anxiety disorder OR	81 (18.1%) 0.52 (0.39–0.7)	256 (22.7%) 0.70 (0.57–0.86)	351 (26.4%) 0.85 (0.70–1.03)	235 (29.6%) 1.00	25.633	<.0005
Mood disorder OR	132 (29.5%) 4.45 (3.23–6.13)	284 (25.2%) 3.60 (2.71-4.77)	229 (17.2%) 2.22 (1.66–2.95)	68 (8.6%) 1.00	124.532	<.0005
Eating disorders OR	14 (3.1%) 0.39 (0.21-0.7)	38 (3.4%) 0.42 (0.28–0.64)	64 (4.8%) 0.61 (0.42- 0.87)	61 (7.7%) 1.00	21.084	<.0005
Personality disorder OR	62 (13.8%) 2.44 (1.64–3.61)	134 (11.9%) 2.05 (1.46–2.88)	118 (8.9%) 1.48 (1.05–2.09)	49 (6.2%) 1.00	27.369	<.0005
Relationship probl. OR	19 (4.2%) 0.21 (0.13- 0.34)	92 (8.2%) 0.42 (0.32–0.56)	169 (12.7%) 0.69 (0.51–0.88)	138 (17.4%) 1.00	68.944	<.0005
Psychosomatic dis. OR	10 (2.2%) 0.67 (0.32–1.41)	29 (2.6%) 0.78 (0.45–1.33)	34 (2.6%) 0.77 (0.46–1.30)	26 (3.3%) 1.00	1.518	.678
Sexual problems OR	4 (0.8%) 0.12 (0.04–0.36)	10 (0.9%) 0.12 (0.06–0.24)	23 (1.7%) 0.24 (0.14–0.39)	55 (6.9%) 1.00	69.369	<.0005
PTSD OR	57 (12.7%) 3.84 (2.41–6.1)	77 (6.8%) 1.93 (1.25–2.99)	72 (5.4%) 1.51 (.97–2.34)	29 (3.7%) 1.00	37.859	<.0005
Unknown	20 (4.5%)	75 (6.7%)	88 (6.6%)	28 (3.5%)	3.640	.303
Total	448	1125	1329	792		

Legend: ADHD = Attention Deficit Hyperactive Disorder; PTSD = Posttraumatic Stress Disorder; CI = Confidence Interval

After assessment with the CAARMS, more patients in class 1 were found to be psychotic than in other classes (7% versus ≤1%). As the probability to be psychotic in class 4 is zero, OR's could not be estimated. Both class 1 and 2 showed a higher prevalence of ARMS (resp. OR= 207.22 and OR= 46.14), whereas the probability of ARMS or psychosis is almost zero in the other two classes. Sex was explored for each class, as previous analyses showed that the distribution of sex was significantly different between the classes and other literature pointed out that young men were more at risk for developing psychosis than women.[4] Also CAARMS-outcome was explored for each class. The percentage of patients who met criteria for an at risk mental state for psychosis was equal for both sexes. However, men were twice more likely to meet CAARMS criteria for psychosis than women, although the chi-square was not significant ($X^2(2, N= 3694) = 4.1, p=.130.$) (1.9% vs. 1% in the overall population, 11.5% vs. 6% in class 1 and 1.5% vs. 0.7% in class 2). Furthermore, the

Figure 4.1: The four classes within a help-seeking population.



Legend Figure 4.1: The four classes within a help-seeking population

Sub scale	LCA item number
Positive symptoms	
perplexity	0-4
thought insertion	5-7
Odd Beliefs/magical thinking	8-12
delusional ideas	13
Ideas of Reference	14-17
Paranoid Ideation	18-20
Grandiosity	21
Perceptual abnormalities	22-24
Auditory hallucinations	25-29
Visual hallucinations	30-33
Somatic hallucinations	34-36
Olfactory hallucinations	37, 38
Conceptual disorganization	39-44
Negative symptoms	
social isolation	45-48
excessive social anxiety	49-51
Avolition	52, 53
decreased expression of emotion	54-58
decreased experience of emotions	59-63
Disorganized symptoms	
Odd behavior or Appearance	64-69
Bizarre Thinking	70
Trouble with focus and attention	71-73
Impairment in personal Hygiene and Social Attentiveness	74-76
General symptoms	
Sleep Disturbance	77
Dysphoric Mood	78-84
Impaired Tolerance to normal stress	85-87
Deterioration in Role Functioning	88-91

GAF scores are lower in class 1 and 2 compared to classes 3 and 4.

Table 4.4: Number of people and odds ratios of screening outcome in the classes

	Class 1: Severe (high risk) N (percent)	Class 2: Moderate (low risk)	Class 3: Mild (very low risk)	Class 4: Normative (no risk)	Chi-square (df=3)	p-value
Male Female OR (Male)	130 (29%) 318 (71%) 0.68 (0.53 – 0.87)	325 (28%) 800 (72%) 0.67 (0.55 – 0.82)	425 (32%) 903 (68%) 0.78 (0.65 – 0.94)	298 (38%) 493 (62%) 1.00	18.323	<.0005
GAF score OR	54.4 (5.3) 0.80 (0.78–8.20)	56,8 (5,7) 0.86 (0.84-8.72)	58.8 (6.2) 0.915 (0.90-0.93)	61.7 (5.8) 1.00	463.01	<.0005
CAARMS interview OR	433 (96.5%) 138.82 (57.1 – 337.44)	367 (32.6%) 107.22 (44.22 – 259.97)	20 (1.5%) 21.05 (8.61 – 51.47)	2 (0.25%) 1.00	1.908	<.0005
ARMS OR	93 (21%) 207.22 (28.77–1492.53)	62 (6%) 46.14 (6.38–333.43)	6 (0,5%) 3.59 (0.43–29.85)	1 (0.1%) 1.00	300.221	<.0005
Psychoses OR*	34 (7%) n.a.	11 (1%) n.a.	1 (0.07%) n.a.	0 (0%) n.a.	114.152	<.0005

Presented odds ratios are the odds of being in class 1 to 3 relative to the odds of class 4 (baseline); CAARMS interview is meeting the criteria for CAARMS interview; * OR is not available due to prevalence 0 in class 4

Discussion

The aim of the present study was to explore the prevalence and latent structure of self-reported psychotic-like experiences in a population of all consecutive young help-seeking patients in secondary mental health services for symptoms of a non-psychotic axis I disorder. We have used the Prodromal Questionnaire to examine the phenomenological underlying latent structure of hypothesized prodromal symptoms. The results support the hypothesis that psychotic-like experiences are common among non-psychotic disorders as almost 97% of the subjects had experienced at least one psychotic-like experience according to the positive symptoms scale of the Prodromal Questionnaire.

The Latent Class Analysis revealed a four-class solution as the best fitting model. The classes were labeled as 'severe', 'moderate', 'mild' and 'normative'. No classes with distinct profiles of psychotic-like experiences were found. These results are in line with a latent class analysis that was conducted in the general population which similarly found four classes of gradually increasing number of psychotic-like symptoms (Murphy et al., 2007). In another study, Shevlin et al. (2007) named

the classes: 'Psychosis' (N=105, 1.8%), 'Hallucinatory' (N=349, 6.0%), 'Intermediate' (N=343, 5.9%) and 'Normative' (N=5,057, 86.4%). However, the 'hallucinatory' class scored lower on hallucinations than the 'psychosis' class and is comparable with our 'moderate' class. Compared to the general population, our results showed much higher proportion of subjects in the more severe classes. This can be explained by treatment-seeking bias. In treatment-seeking populations the co-morbidity of symptoms and disorders is larger than in the general population, because symptoms all independently contribute to help-seeking behavior. Psychiatric syndromes are associated with psychotic-like experiences, lower psychosocial functioning, help-seeking behavior and distress and are therefore more represented in this clinical population (Addington, Van Mastrigt, Hutchinson & Addington, 2002; Rosen, Miller, D'Andrea, McGlashan & Woods, 2006; Svirskis et al., 2005).

The pattern of endorsing items, showed a gradual increase of negative, disorganized and general symptoms, which suggest a continuum for negative symptoms as well. This is in line with the findings that negative symptoms precede the onset of psychotic-like experiences and psychosis (Cornblatt et al., 2003; Klosterkötter, Hellmich, Steinmeyer & Schultze-Lutter, 2001). The higher proportion of females in classes 1 and 2 reflects the sex ratio found in all help-seeking persons in the secondary mental health services in The Hague. Although not significant, men were twice more likely than women to meet CAARMS criteria for psychosis. The risk of having an at-risk mental state was equal for men and women. Most publications with referred samples report a higher proportion of males (Cornblatt et al., 2003; Klosterkötter et al., 2001; Yung et al., 2006). Referral to services for psychosis might be a biased process selecting young males with predominantly negative and cognitive symptoms. This reduced social competence may draw attention of parents and teachers in schools or work colleagues and lead to referral to a specialized psychosis clinic in many cases. In female patients the psychotic-like symptoms have been found to be associated with emotional problems, social conflicts and help-seeking behavior (Van Os, Kenis & Rutten, 2010) and referral to secondary mental health services in contrast to specialized psychosis clinics may be more likely. In addition, the present study was not restricted to schizophrenia, were male patients predominate, but also assesses depression with psychotic features and bipolar disorder. Here, women are more prevalent.

The four classes show a consistent increase in the probability of endorsing any item. This could support the concept of a continuum of psychosis. Kaymaz and Van Os (2010) hypothesized that a latent construct divides this apparent continuum

in two groups: one with psychotic experiences in the context of cognitive and motivational impairment that have a high probability of need for care for these experiences, and one group that has psychotic-like experiences of a different origin, that is associated with a lower probability of need for care for these experiences.

Strengths and limitations

The usage of the Prodromal Questionnaire (Loewy et al., 2005) to measure PLEs has some limitations. Firstly, we used the original Prodromal Questionnaire that did not include distress and frequency. It is known that the onset of psychosis is mediated by distress and frequency of the symptoms (Kaymaz & van Os, 2010; Yung et al., 2006). Secondly, persistence of symptoms is predictive for psychosis, but we did not collect any information on the duration or persistence of symptoms. Thirdly, items could be misunderstood by patients due to the nature of the statements. This misunderstanding could contribute to over-rating. Fourthly, as this is a self-report questionnaire, patients could be more likely to give a false representation of their symptoms, resulting in over-rating or under-rating of the symptoms.

A further limitation is that membership to the different latent classes is not an all or nothing phenomenon. Membership to a class is based on the likelihood of membership for every class, estimated by the model for each individual. However, in our study the measure of classification quality was very high (0.962-1.0) meaning that all subjects could be classified with a high certainty to only one class.

The study has also a number of strengths. Latent class analysis has several additional advantages over traditional cluster analyses methods such as k-means clustering. Latent class analysis is more objective, because it does not use a clustering algorithm and so the choice of clustering algorithm and its effects on results is not an issue. The quality of classification based on posterior probabilities can be assessed. In addition, the number of classes in the data can be determined, because latent class analysis is based on a statistical model. This makes the method more objective, since the classes are not based on the assumptions of researchers. Unlike cluster analyses, latent class analysis does not need to fulfill the assumption of normally distributed data. Furthermore, the analysis can include a mix of nominal, ordinal or continuous variables.

Another strength of this study is that, to our knowledge, it is the first to explore not only the positive experiences, but also the other sub-clinical symptoms of psychosis in an epidemiologically representative sample of all consecutively help-seeking people in a well-defined urban catchment area. High prevalences of social disability, negative symptoms and cognitive impairments are present before the

onset of psychotic-like experiences and have been found to predict psychosis in 37 percent of patients over a ten-year period (Cornblatt et al., 2003; Klosterkötter et al., 2001; Velthorst et al., 2009).

Conclusion and implications

Our findings suggest that the psychosis phenotype differs along a psychosis continuum and is divided in underlying latent classes. The presence of psychotic-like experiences is accompanied by a mixture of general psychopathology, and specific developmental and psychological contexts in the development of psychosis. Therefore, screening at the level of the need for care would be an effective and productive strategy for early detection (Howes & Kapur, 2009). Patients seeking help for mental problems who also experience prodromal symptoms are more likely to be distressed and disturbed by these symptoms. A closing-in detection strategy in a general help-seeking population that combines several risk-factors is a promising strategy to detect patients that have a certain risk for developing psychosis (McGorry, Yung & Phillips, 2003). As PLEs are quite common in the patient population, it is important to explore the differences between those patients who develop psychosis and those who do not. Analyses that focus on underlying latent classes will contribute to an understanding of the etiology (why some psychotic-like experiences precede psychosis, whereas others do not) and the development of screening tools with higher sensitivity and specificity.

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Additional Table 4.1: Adjusted standard residuals for care programmes across classes

	Class 1 Severe (high risk)	Class 2 Moderate (low risk)	Class 3 Mild (very low risk)	Class 4 Normative (no risk)	χ^2
Attention Deficit Hyperactive disorder					χ^2 (3, 3694)= 3,6 p=.307
Anxiety disorders	▼	▼		▲	χ^2 (3, 3694)= 25,1, p<.0005
Mood disorders	▲▲	▲▲	▼	▼▼▼	χ^2 (3, 3694)= 17,26, p<.0005
Eating disorders	▼			▲	χ^2 (3, 3694)= 22,36, p<.0005
Personality disorders	▲	▲		▼	χ^2 (3, 3694)= 26,84, p<.0005
Posttraumatic stress disorder	▲▲			▼	χ^2 (3,3694)= 42,55, p<.0005
Relationship problems	▼▼	▼	▲	▲▲	χ^2 (3,3694)= 65,43, p<.0005
Psycho-somatic disorders					χ^2 (3,3694)= 1,57, p=.667
Sexual disorders	▼	▼	▼	▲▲▲	χ^2 (3,3694)= 84,45, p<.0005

▼ ▼▼ or ▲▲▲: adjusted standardised residuals > |7,5|

▼▼ or ▲▲ : adjusted standardised residuals > |5|

▼or ▲: adjusted standardised residuals > |2|

Legend: chi-square cross-tabulation analysis between the initial disorder and psychotic disorder sub group diagnosis in which adjusted standardized residuals reflect a higher or lower number of cases than expected, corrected for small N. Negative adjusted residuals in a cell correspond to a smaller number of cases than expected by chance, positive residuals to more cases. Adjusted standardized residuals outside the range −2.0 and +2.0 indicate significant differences between observed and expected numbers.

Additional table 4.2: Adjusted standardized residuals outcome screening of classes compared to the normative class

	Class 1 Severe (high risk)	Class 2 Moderate (low risk)	Class 3 Mild (very low risk)	Class 4 Normative (no risk)	χ^2
Male				▲	χ^2 (3,3692)= 18,551, p<.0005
Meet criteria for interview	▲▲▲	▲▲▲	▼▼▼	▼▼▼	χ^2 (3,3694)= 2055,517, p<.0005
Not Arms	▼▼▼		▲▲▲	▲▲▲	χ^2 (3,3694)= 546,998, p<.0005
ARMS	▲▲▲	▲	▼▼▼	▼▼	χ^2 (3,3694)= 373,144, p<.001

▼ ▼▼ or ▲▲▲: adjusted standardised residuals > |7,5|

▼▼ or ▲▲ : adjusted standardised residuals > |5|

▼or ▲: adjusted standardised residuals > |2|

ARMS = At Risk Mental State; Chi-square cross-tabulation analysis between the initial disorder and psychotic disorder sub group diagnosis in which adjusted standardized residuals reflect a higher or lower number of cases than expected, corrected for small N. Negative adjusted residuals in a cell correspond to a smaller number of cases than expected by chance, positive residuals to more cases. Adjusted standardized residuals outside the range −2.0 and +2.0 indicate significant differences between observed and expected numbers.